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UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

ADAPT PHARMA OPERATIONS LIMITED, ADAPT PHARMA INC., ADAPT PHARMA LIMITED, and OPIANT PHARMACEUTICALS, INC., Plaintiffs, v. TEVA PHARMACEUTIALS USA, INC. and TEVA PHARMACEUTIALS INDUSTRIES, LTD. Defendants.	Civil Action No. 16-7721 (BRM)(JAD) (Consolidated)

PLAINITFFS' BRIEF REGARDING THE PETITIONS FOR INTER PARTES REVIEW OF THE PATENTS-IN-SUIT

The recent institution decisions of the Patent Trial and Appeal Board fatally undermine Teva's contention that the asserted claims of the patents-in-suit are obvious. The Board addressed the same obviousness issues that are before this Court and applied a much lower standard of proof than the clear-and-convincing standard Teva faces here. It concluded that there was not even a "reasonable likelihood" that the petitioner, Nalox-1 Pharmaceuticals, LLC, could prevail as to any of the claims requiring benzalkonium chloride (BZK), because Wyse (TX-0048), about which this Court heard extensive testimony at trial, taught away from its use. For Teva to prevail here, it needs to persuade this Court to adopt exactly the opposite position as the Board. Although the decisions of the Board are not binding here, its judges have subject-matter expertise, *see Belden Inc. v. Berk-Tek LLC*, 805 F.3d 1064, 1079 (Fed. Cir. 2015), and its "findings are trustworthy and probative of the issues," *Procter & Gamble Co. v. Team Techs., Inc.*, 2014 WL 12656554, at *10 n.4 (S.D. Ohio July 3, 2014). As Plaintiffs explain in their trial brief, the record here only confirms that the Board's non-obviousness determinations were correct and that Teva cannot possibly establish obviousness of any of the asserted claims.

I. Background: The Patent Trial and Appeal Board and the Nalox-1 Petitions

An *inter partes* review ("IPR") is a proceeding in which a panel of three administrative patent judges is tasked with reviewing the patentability of a previously issued patent. To request an IPR, a petitioner files a brief explaining why the claims should be found anticipated or obvious, along with written testimonial evidence. Based on that submission (and an optional response), the Board makes a preliminary decision whether to "institute" an IPR. 35 U.S.C. § 314. Initially, the Board must make a threshold determination that "there is a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition." *Id.* § 314(a). If it institutes, the Board then receives further written submissions, typically hears oral argument, and ultimately issues a "final written decision." *Id.* § 318(a).

The "reasonable likelihood" standard imposes a far lower burden of proof on petitioner as compared to Teva's burden in this case to prove obviousness by "clear and convincing evidence." 35 U.S.C. § 273(b); *Procter & Gamble*, 2014 WL 12656554, at *10. The Board ultimately decides patentability by a preponderance of the evidence; at institution, the question is not even whether the petitioner has met this burden, but merely whether it has a reasonable likelihood of success in ultimately doing so. *E.g.*, *Nestlé Purina Petcare Co. v. Oil-Dri Corp. of Am.*, IPR2015-00737, Paper 16, at 2 (P.T.A.B. Sept. 23, 2015). Crucially, when the Board grants institution, it is required to institute a petition in its entirety—on *all* challenged claims—even if the petitioner has shown a reasonable likelihood of invalidating only *one* claim. The Board may not institute a petition only in part. *SAS Inst., Inc. v. Iancu*, 138 S. Ct. 1348, 1354 (2018).

Nalox-1 filed a total of fifteen petitions for IPR: three against each of the four patents-in-suit before this Court (U.S. Patent Nos. 9,468,747 ("the '747 patent"), 9,561,177 ("the '177 patent"), 9,269,965 ("the '965 patent"), and 9,775,838 ("the '838 patent")), plus three against no-longer-asserted U.S. Patent No. 9,211,253 ("the 253 patent").[1] For each patent, Nalox-1 filed one petition with the Wyse patent (TX-0048) as the lead reference, one with Davies (TX-3109) as the lead, and one with a reference called Wang (not before this Court) as the lead reference.[2] The arguments in each petition, however, were substantially similar to each other and to the arguments Teva made before this Court. In each petition, Nalox-1 cited not only Wyse (TX-0048) and Davies (TX-3109), but also Djupesland (TX-3007), Kerr 2009 (TX-0029), and Bahal (TX-3009)—*i.e.*, references that were the focus of trial and which include references that Teva

[1] Nalox-1 challenged all claims of each patent, so the ten claims at issue in this case (claims 7 and 9 of the '747 patent, claim 4 of the '177 patent, claims 21, 24, and 25 of the '965 patent, and claims 2, 24, 33, and 38 of the '838 patent) are a subset of the claims in Nalox-1's petitions.

[2] For the Court's convenience, these differences and the status of each petition are summarized in **Appendix A**.

asserted in its obviousness "combinations." Recognizing that Nalox-1's arguments were largely the same across all of the IPRs, the Board exercised its discretion to deny all the petitions except some of the ones based on Wyse. *See, e.g.*, *Nalox-1 Pharms., LLC v. Opiant Pharms., Inc.*, IPR2019-00689, Paper 11, at 10–11 (P.T.A.B. Sept. 9, 2109).

Of the "Wyse" petitions, the Board denied the petitions relating to the '177 and '838 patents, and instituted review of the '253, '747, and '965 patents. In every case, however, the Board's reasoning was essentially the same. Like Teva here, Nalox-1 contended that it would have been obvious to the person of ordinary skill in the art (POSA) to arrive at Plaintiffs' claimed formulation, including the combination of naloxone with BZK and EDTA. In each case, however, the Board disagreed because it concluded that Wyse teaches away from the use of BZK in naloxone formulations because—just as Plaintiffs' expert Dr. Illum opined at trial—"Wyse teaches away from using [BZK], and especially with EDTA, in formulating intranasal naloxone." *E.g.*, *Nalox-1 Pharms., LLC v. Opiant Pharms., Inc.*, IPR2019-00688, Paper 11 at 22 (P.T.AB. Sept. 9, 2019) ("'747 Wyse ID"). The Board instituted only on those patents having claims that were not limited to BZK specifically, and even then it expressly recognized that Nalox-1 had not shown a reasonable likelihood of success as to any claims reciting BZK. *Id*. at 23–24. It instituted on all claims in these patents only because it was required to do so under *SAS*. *Id*.

II. The Board's Finding that Wyse Teaches Away from BZK Undermines Teva's Case.

The Board's conclusions regarding BZK confirm that Teva's obviousness case is fatally flawed. The Board focused on and found persuasive the very same passages of Wyse addressed by Plaintiffs' expert Dr. Illum, in which Wyse reported that his formulation studies "surprisingly showed that the use of benzalkonium chloride, a common nasal product preservative, resulted in an additional degradant," and from which Wyse concluded that BZK was not "acceptable" as a preservative "due to increased observed degradation." '747 Wyse ID at 20 (quoting Wyse (TX-

0048) at 27:29–32, 27:42–44); *see also* Trial Tr. 672:12–675:20. The Board acknowledged that Wyse designated the study involving BZK as "preliminary," but contrary to Teva's arguments did not find this to be a reason to discredit it; although Wyse may not have "conclusively determine[d]" the cause of the additional degradant, it was sufficient for Wyse to "criticize, discredit, or otherwise discourage" the POSA from BZK for the reference to teach away. '747 Wyse ID at 20. The Board also rejected the argument regarding Wyse's omission of formulation 12 from the list of unstable BZK-containing formulations and instead found that "formulation 12 does not negate Wyse's explicit statement discrediting [BZK] as an excipient in intranasal naloxone formulation[s]." *Id.* at 21.

For Teva to prevail, it must persuade this Court to come to conclusions regarding Wyse that the Board rejected, despite Teva's much higher burden of proof. The Board found that Nalox-1 lacked *even a reasonable likelihood* that it could establish, *by a preponderance*, that Wyse does not teach away. Here, Teva must establish that Wyse dose not teach away *by clear and convincing evidence*.[3] The Board's analysis of the BZK issue, though non-binding, is powerful evidence that Plaintiffs should prevail. Moreover, Plaintiffs are entitled to final judgment in this case if they can prevail on any one claim—and on five of the ten at issue (claim 4 of the '177 patent and claims 2, 24, 33, and 38 of the '838 patent) the Board did not institute an IPR *at all*. And as to three more (claims 7 and 9 of the '747 patent and claim 21 of the '965 patent), the Board expressly found that the claims did not meet the institution threshold, but nevertheless granted institution as required under *SAS* because of other claims in those patents.

[3] Although the initial burden to come forward with a proffered teach away is Plaintiffs', plainly they have met that burden; the ultimate burden of persuasion remains with Nalox-1 in the IPRs and with Teva here. *In re Magnum Oil Tools Int'l, Ltd.*, 829 F.3d 1364, 1376 (Fed. Cir. 2016).

III. The Board's Findings Regarding Dose Do Not Help Teva.

The Board also addressed Nalox-1's arguments regarding the obviousness of a 4 mg dose—an issue that was also a focus of Teva's presentation at trial. But on this issue, the Board's findings are much less relevant to the proceedings in this Court. Unlike on BZK, where the Board decided not to institute at all on two of the patents because the art taught away from using BZK, the Board made no final determinations regarding dose. Nalox-1's dose arguments, unlike Teva's, did not center not around Davies (TX-3109) or Strang (TX-0054), but rather on various pharmacokinetic calculations that Nalox-1 made from the disclosures of Wyse. '747 Wyse ID at 17. The Board expressed "doubt" about these calculations, but concluded that "these factual issues, together with evidence of secondary considerations, are better suited for evaluation after the parties fully develop the record during trial." *Id.* at 18. Notably, Plaintiffs' principal response and supporting evidence to Nalox-1's petitions—on both BZK and dose—have not yet been filed, and, at the institution stage, the Board is required to presume facts in favor of the petitioner. *See, e.g.*, 37 C.F.R. § 42.108. In other words, the Board's preliminary decisions in favor of Nalox-1 rested on the low evidentiary threshold for institution, as well as the particulars of Nalox-1's arguments and a necessarily underdeveloped record.

Here, the Court has a fully developed trial record, and unlike the Board at institution, it is well positioned to evaluate—and reject—Teva's specific arguments, for all the reasons Plaintiffs have explained in their trial brief. And even leaving aside the entire question of the naloxone dose, the teach away on BZK, without more, suffices to entitle Plaintiffs to judgment.

For all of these reasons, this Court should decide the BZK issue the same way the Board did and reject Teva's obviousness arguments because the art (Wyse in particular) taught away from the use of BZK and BZK combined with EDTA. As to the remaining elements of the claims, they too are non-obvious, as was evident at trial.

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Respectfully submitted,

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APPENDIX A: CHART OF NALOX-1 IPR PETITIONS

IPR Case No.	Challenged Patent	Prior Art	Instituted?
IPR2019-00685	9,211,253	Wyse	Yes
IPR2019-00686	9,211,253	Wang	No
IPR2019-00687	9,211,253	Davies	No
IPR2019-00688	9,468,747*	Wyse	Yes
IPR2019-00689	9,468,747*	Wang	No
IPR2019-00690	9,468,747*	Davies	No
IPR2019-00691	9,561,177*	Wyse	No
IPR2019-00692	9,561,177*	Wang	No
IPR2019-00693	9,561,177*	Davies	No
IPR2019-00694	9,269,965*	Wyse	Yes
IPR2019-00695	9,269,965*	Wang	No
IPR2019-00696	9,269,965*	Davies	No
IPR2019-00697	9,775,838*	Wyse	No
IPR2019-00698	9,775,838*	Wang	No
IPR2019-00699	9,775,838*	Davies	No

* Patent asserted against Teva in this litigation.

CERTIFICATE OF SERVICE

I hereby certify that on November 13, 2019, I caused a true and correct copy of the foregoing to be served on all counsel of record via CM/ECF and email.

/s/ Charles H. Chevalier
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